PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis*.3(c) and 72.2)

To:

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JAPON

Date of mailing *(day/month/year)* 31 August 2006 (31.08.2006)	
Applicant's or agent's file reference N13F1456	**IMPORTANT NOTIFICATION**
International application No. PCT/JP2004/018719	International filing date *(day/month/year)* 15 December 2004 (15.12.2004)
Applicant NAKAMURA, Toshikazu et al	

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yoshiko Kuwahara Facsimile No. +41 22 338 82 70

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference N13F1456	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2004/018719	International filing date *(day/month/year)* 15 December 2004 (15.12.2004)	Priority date *(day/month/year)* 16 December 2003 (16.12.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant NAKAMURA, Toshikazu		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 22 August 2006 (22.08.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yoshiko Kuwahara e-mail: pt07@wipo.int

PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference **N13F1456**	Date of mailing *(day/month/year)* **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/018719	**15.12.2004**	**16.12.2003**

International Patent Classification (IPC) or both national classification and IPC

Applicant
NAKAMURA, Toshikazu

1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP Facsimile No.	Authorized officer Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/018719

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☒ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/018719

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

This authority finds that the common subject matter of claims 1-18 is a sugar chain-lacking hepatocyte growth factor characterized by a hepatocyte growth factor wherein the sugar chains are lacking at all or at least one of the sugar chain attachment sites, and matters related to the same.

However, Biochim. Biophys. Acta., 1992, 1120(3), p. 343-50 describes a sugar chain lacking hepatocyte growth factor wherein the sugar chains are lacking at all or at least one of the sugar chain attachment sites, and therefore because the aforementioned subject matter is described in this document, it is not novel.

In other words, the above common subject matter does not go beyond the scope of prior art, and therefore cannot be considered a common technical feature in the sense of the second sentence of PCT Rule 13.2.

This being the case, the above claims in their entirety lack common subject matter, and because no other common subject matter that can be considered a common technical feature in the sense of the second sentence of PCT Rule 13.2 exists, no technical relationship can be found among these inventions that differ from each other in the sense of PCT Rule 13.

As a result, it is clear that the inventions of claims 1-18 do not satisfy the requirement for unity of invention.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☒ all parts

   ☐ the parts relating to claims Nos. _____

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/018719

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2-3, 5-7, 9-13, 15-18	YES
	Claims	1, 4, 8, 14	NO
Inventive step (IS)	Claims		YES
	Claims	1-18	NO
Industrial applicability (IA)	Claims	1-18	YES
	Claims		NO

2. Citations and explanations:

Document 1: Biochim. Biophys. Acta., 1992, 1120(3), p. 343-50
Document 2: Miyazawa K. et al., Human hepatocyte growth factor (hHGF) mRNA, complete cds. Database GenBank accession No. M29145, November 8, 1994
Document 3: Proc. Natl. Acad. Sci. USA, 1991, 88(16): 7001-5
Document 4: JP 7-508420 A (Genentech Inc.) 21 September 1995
Document 5: J. Biochem. (Tokyo), 1993, 114(1), p. 76-82

The inventions of claims 1, 4, and 15 lack novelty with respect to document 1 cited in the international search report.

Document 1 describes a sugar chain-lacking hepatocyte growth factor obtained by the action of an enzyme having cleaving activity toward sugar chains such as N-glycanase and the like on wild type Scatter factor (corresponding to the hepatocyte growth factor of this application).

The invention of claim 8 lacks novelty with respect to documents 2 and 3 cited in the international search report.

The DNA that encodes the sugar chain-lacking hepatocyte growth factor described in document 1 may also be a wild type gene, and therefore the DNA of claim 8 also includes DNA encoding wild type hepatocyte growth factor.

Document 2 describes DNA that encodes the hepatocyte growth factor represented by the amino acid sequence identified as SEQ ID NO: 1 of this application, and document 3 described DNA that encodes the hepatocyte growth factor represented by the amino acid sequence identified as SEQ ID NO: 2 of this application (for document 3, see Database GenBank accession No. M73240).

(Continued in Supplemental Box)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/018719

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box V.

The inventions of claims 2, 3, 5-7, 9-13, and 15-18 lack an inventive step with respect to documents 1-5 cited in the international search report.

Document 4 describes the use of host cells such as E. coli and the like for the expression of various hepatocyte growth factor mutants, and it describes the chemical or enzymatic removal of carbohydrate groups (corresponding to the sugar chains in this application) that are present on the hepatocyte growth factor mutants (especially page 8, lower left column, line 28 to page 9, lower left column, line 3).

Document 5 describes the sugar chain attachment sites on hepatocyte growth factor (especially, page 76, left column, lines 13 to 16).

At the time this application was filed, the investigation of the biochemical function of sugar chains in various glycoproteins was a widely known issue, and it was widely known technology to prepare those proteins wherein all or part of the sugar chains were lacking either by blocking the attachment of the sugar chains through point mutations in the amino acid residues involved in sugar attachment, or by using enzymes having sugar chain cleaving activity on proteins with attached sugar chains (for example, J. Cell. Biol., 1993, 121(3), p. 705-13; Biosci. Biotechnol. Biochem., 1998, 62(7), p. 1318-25; J. Biol. Chem., 1991, 266(17), p. 11051-7; Growth Factors, 2001, 19(2), p. 127-43). In addition, the use of hepatocyte growth factor in medicine was also widely known technology.

As a result, this authority finds that persons skilled in the art could easily conceive of investigating the biochemical function of the sugar chains in hepatocyte growth factor, which is a glycoprotein, and based on the inventions described in documents 1-5 and the aforementioned widely known technology, persons skilled in the art could easily prepare a sugar chain-lacking hepatocyte growth factor by introducing a mutation in the amino acid sequence at one or more sugar chain attachment sites of hepatocyte growth factor such that the sugar chain could not attach by utilizing the sequence data concerning sugar chain attachment sites in hepatocyte growth factor described in documents 2 and 3, and the data concerning the sugar chain attachment sites of hepatocyte growth factor described in document 5. Furthermore, using a cell free protein synthesis system that was widely known at the time this application was filed as the protein expression system is merely a matter to be achieved as needed by persons skilled in the art.